PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 705473-6001	**FOR FURTHER ACTION** see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT/US07/08021	International filing date (*day/month/year*) 30 March 2007 (30.03.2007)	(Earliest) Priority Date (*day/month/year*) 31 March 2006 (31.03.2006)
Applicant HUMAN GENOME SCIENCES, INC.		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 6 sheets.

☐ It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the Report**
   a. With regard to the **language**, the international search was carried out on the basis of:
      ☒ the international application in the language in which it was filed.
      ☐ a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b))
   b. ☐ This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 Rule 43.6 *bis(a)*
   c. ☒ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.
2. ☐ **Certain claims were found unsearchable** (See Box No. II)
3. ☒ **Unity of invention is lacking** (See Box No. III)
4. With regard to the **title**,
   ☒ the text is approved as submitted by the applicant.
   ☐ the text has been established by this Authority to read as follows:

JMG LAE

LEYDIG, VOIT & MAYER
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AUG 0 7 2008
PAY/TM Due Date

5. With regard to the **abstract**,
   ☒ the text is approved as submitted by the applicant.
   ☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.
6. With regard to the **drawings**,
   a. the figure of the **drawings** to be published with the abstract is Figure No. _____
      ☐ as suggested by the applicant.
      ☐ as selected by this Authority, because the applicant failed to suggest a figure.
      ☐ as selected by this Authority, because this figure better characterizes the invention.
   b. ☒ none of the figures is to be published with the abstract.

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Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of:

   a. type of material

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material

   ☒ on paper

   ☒ in electronic form

   c. time of filing/furnishing

   ☒ contained in the international application as filed

   ☒ filed together with the international application in electronic form

   ☐ furnished subsequently to this Authority for the purposes of search

2. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

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Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of any additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-10

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

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A. CLASSIFICATION OF SUBJECT MATTER
IPC: **C12N 5/20**(2006.01);**C07K 16/00**(2006.01);**G01N 33/53**(2006.01)

USPC: 435/326,331,7.1;530/387.1,387.3,388.1
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 435/326,331,7.1;530/387.1,387.3,388.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
STIC (sequences), EAST, STN (Medline, Biosis)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2005/0186637 (YU et al.) 25 August 2005 (25.08.2005), claims 1-10.	1-10

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search
17 July 2008 (17.07.2008)

Date of mailing of the international search report
04 AUG 2008

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Form PCT/ISA/210 (second sheet) (April 2007)

BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1-10, drawn to a hybridoma, the antibody secreted thereby, and a method of detecting Neutrokine-α protein with the antibody.

Group II, claim(s) 11, 12 and 14, drawn to an isolated protein comprising Neutrokine-α protein fused to a toxin protein, and use of the protein for the preparation of a medicament.

Group III, claim(s) 13, drawn to an in vitro method of killing a B lymphocyte with the fusion protein.

Group IV, claim(s) 15 in part and claim 16, drawn to a method of treating a B cell cancer with the antibody.

Group V, claim(s) 15 in part and claims 17-24, drawn to an autoimmune disease with the antibody.

Group VI, claim(s) 25-28, drawn to a method of reducing the frequency or quantity of corticosteroid by administering the antibody.

Group VII, claim(s) 29 in part and claim 30, drawn to a method of treating a B cell cancer with the fusion protein.

Group VIII, claim(s) 29 in part and claim 31, drawn to an autoimmune disease with the fusion protein.

The inventions listed as Groups I-VIII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

This Authority considers that the main invention in the instant application comprises the first-recited product, a hybridoma, the antibody secreted thereby, and the first-recited method of using the antibody, namely, a method of detecting Neutrokine-α protein with the antibody. Note that there is no method of making the hybridoma. The additional protein product of Group II is a distinct chemical entity from the hybridoma/antibody of Group I, and therefore, they do not share the same technical feature with the main invention within the meaning of PCT Rule 13.2, so as to form a single general inventive concept.

Further, methods of groups III, VII and VIII does not correspond to the main invention, as it is drawn to a method of using a Neutrokine-α fusion protein, which is neither a method of making, nor a method of using said hybridoma or antibody. Therefore, the two groups are not considered to share a special technical feature within the meaning of PCT Rule 13.2, and thus do not relate to a single invention concept within the meaning of PCT Rule 13.1.

Furthermore, the inventions listed as Group I and Groups IV-VI do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features because of the following: 37 CFR 1.475(d) states that if multiple products, processes of manufacture or uses are claimed, the first invention of the category first mentioned in the claims of the application and the first recited invention of each of the other categories related thereto will be considered as the main invention in the claims, see PCT Article 17(3)(a) and 1.476 (c). Claim 10 drawn to the first method of using the product of claim 1 and is grouped with the product as the main invention. Group IV requires the "special technical feature" such as that it requires killing B lymphocyte, which is not required for the method in Group I. The method in Group I requires the "special technical feature" of detecting

the Neutrokine-α protein, which is not required for the method of Group IV. Groups V and VI require the "special technical feature" such as that they are carried out in vivo, and require the step of administering the antibody to a patient, which are not required for the method in Group I. The method in Group I requires the "special technical feature" of detecting the Neutrokine-α protein in vitro, which is not required for the methods of Groups V and VI. As such, unity is lacking between Group I and Groups IV-VI.

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In order for more than one species to be examined, the appropriate additional examination fees must be paid. The species are as follows:

Species 1-5: non-Hodgkin's lymphoma; multiple myeloma; CLL; ALL; and plasmacytoma, respectively;

Species 6-14: SLE; MS; myasthenia gravis; Sjogren's syndrome; type 1 diabetes; idiopathic thrombocytopenia purpura; Gullian-Barre syndrome; Hashimoto's thyroiditis; and Graves' disease; respectively;

Species 15: rheumatoid arthritis.

The claims are deemed to correspond to the species listed above in the following manner:

Claims 16 and 30 - Species 1-5;
Claims 17 and 31 - Species 6-14;
Claim 28 – species 6, 9 and 15.

The following claim(s) are generic: claim 15 is generic for claims 16 and 17; claim 25 is generic for claim 28; claim 29 is generic for claims 30 and 31.

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons:

Each species set forth above has distinct clinical pathology, manifestation and prognosis, and therefore, these species do not share a special technical feature within the meaning of PCT Rule 13.2, and thus do not relate to a single invention concept within the meaning of PCT Rule 13.1.